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Applicant(s):	Orhun K. MURATOGLU et al.	Confirmation No.: 3038
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Title:	METHODS FOR MAKING OXIDATION RESISTANT POLYMERIC MATERIAL	

Commissioner for Patents
U.S. Patent and Trademark Office
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DECLARATION OF ORHUN K. MURATOGLU

I, Orhun K. Muratoglu, do hereby declare as follows:

1. I received my Ph.D. in Materials Science and Engineering, Program in Polymer Science and Technology, from the Massachusetts Institute of Technology ("MIT") in 1995. I have been engaged in the study of polymers, such as ultra high molecular weight polyethylene (UHMWPE), for use in medical implants for over 12 years. I have authored or co-authored at least 45 peer-reviewed articles and 14 book chapters and review articles concerning cross-linked and wear resistant UHMWPE and methods of making such UHMWPE for medical implants. I am currently the co-director of the Harris-Orthopedic Biomechanics and Biomaterials Laboratory at the Massachusetts General Hospital. A copy of my *curriculum vitae* accompanies this declaration.

2. I provide this declaration to explain the nature of the problems (both generally known and not generally known) encountered in prosthetic replacements in the orthopedics field, the prior art attempts at solving these problems, the differences between our invention and the prior art, and the advantages provided by our invention over the prior art. Prosthetics replacements are used in a wide variety of contexts. Notable examples are in the hip and the knee. In this declaration, I focus upon the hip.

3. Slide 1 depicts a hip replacement scenario at pre-operation and post-operation stages. The PreOp photograph shows a damaged hip socket region. The PostOp slide shows a hip prosthetic that includes the (i) metal (titanium or cobalt chrome) femur insert and cobalt chrome ball and (ii) the ultrahigh molecular weight polyethylene (UHMWPE) liners, which are affixed to the hip. The photograph on the right shows an assembly prior to implantation. A typical patient requiring a hip replacement is usually 60 years old or over, although hip surgeries are often performed in young adults, particularly due to osteoarthritis, accidents or congenital defects.

4. Slides 2 and 3 depict one problem associated with conventional UHMWPE prostheses, most of which are subjected to terminal radiation sterilization (usually about 25 kGy). Slide 2 is an illustration of a wear phenomenon. Over time, conventional UHMWPE used in hip prostheses would wear and generate micron-sized particle debris. This is thought to occur by the formation of fibrils that are sheared by the forces in the joint to form small particles. These particles would be recognized by macrophages as foreign, and the macrophages would attempt to destroy the particles. In this process, the macrophages would express a variety of proteins, including cytokines. The proteins would stimulate cells known as osteoclasts. Osteoclasts remove bone tissue by a process called bone resorption. Slide 3 at the arrows show actual bone resorption, which will ultimately result in loosening of the implant components, eventual bone fracture and breakage, and require a revision surgery on the patient. The typical time for the need for a revision surgery due to bone resorption induced by wear particles is 10-15 years after initial implantation. Thus, the typical patient who received an implant in their 60's could expect to require a revision surgery in their 70's to 80's.

5. There is another problem with conventional UHMWPE that is terminally sterilized with radiation. The irradiation process generates free radicals in the polymer. These free radicals can react with oxygen found in the synovial fluid to form peroxy free radicals. Peroxy free radicals will abstract a hydrogen atom from another polymer molecule forming

a hydroperoxide and another free radical. The newly generated free radical will go on to continue to the oxidation cascade, which is a chain reaction. The hydroperoxides are unstable, and will result in chain scission of the UHMWPE polymer molecules. This will ultimately result in embrittlement, which in turn causes delamination and failure of the implant. The photograph in slide 4 shows the oxidation damage in an implant retrieved after a revision surgery.

6. Revision surgery is a major surgery, particularly for elderly patients. See slide 5. Surgeries can easily be 10-12 hours long with the patient under full anesthesia. The failed implant must be removed, and replaced with a larger one to compensate for bone destroyed by the osteoclasts. Often bone grafts also are required. The outcomes of revision surgeries can be quite varied and can present significant risk and expense due to the age of the patient, the stress of the surgery, the need for bone grafts and the significant amount of time that the patient is under anesthesia. Thus, there has been a very real need to reduce or eliminate bone destruction, implant failure and occurrence of revision surgeries. See slide 6.

7. The first attempt to solve this problem is depicted in slides 7-10. Turning first to slide 7, the left side shows a scanning electron micrograph of a failed liner made of conventional irradiated UHMWPE. This micrograph shows the fibrils formed in the UHMWPE, which are then thought to be sheared off by forces in the hip joint to form micron-sized UHMWPE particles. The right side show what occurs with irradiation cross-linking. Unirradiated UHMWPE shows a wear rate of almost 10 mg/MC (MC = million cycles), and those sterilized with irradiation (25 kGy) are slightly lower, about 9 mg/MC. At a radiation level of about 175 kGy, about seven times the sterilization doses, the wear drops to less than 1 mg/MC.

8. However, as stated previously, radiation creates free radicals. More particularly, UHMWPE contains lamella-like crystallites, where the chain is in a highly ordered state, as schematically shown Slide 8. Between these crystalline regions are amorphous regions,

where the chain is in a disordered state, as schematically shown slide 8. When polyethylene is below the melting point, the amorphous regions connect crystallites to one another.

9. Ionizing radiation (electron and gamma ray) cleaves the C-H bonds of polyethylene, thereby causing the formation of a carbon free radical along the backbone of the polymer chain. Free radicals are atoms that contain unpaired electrons in the outermost electron shell. A free radical seeks to pair up its unpaired electron with another unpaired electron, which can be done by sharing an electron with another free radical and forming a covalent bond. The interaction between two free radicals results in each sharing an electron with the other such that there is a pair of shared electrons between the atoms. This sharing of electrons in this manner results in the elimination of two free radicals for every bond formed. Thus, the use of ionizing irradiation results in the formation of covalent bonds, which in the context of UHMWPE forms cross-links between polymer chains and within polymer chains. See bottom left corner of slide 8.

10. If the polymer is irradiated at a temperature below the melting point, such radiation generates free radicals (☆) from atoms randomly throughout the irradiated polymer, irrespective of the crystal morphology, as schematically shown in the middle of slide 8. Accordingly, free radicals are generated both in the crystalline and the amorphous regions of the UHMWPE by irradiation. A pair of shared electrons formed by recombination between the free radicals results in a covalent bond between the two atoms, and such a bond is a cross-link in the context of UHMWPE (●).

11. Reactivity of the irradiation-generated free radicals is much higher in the amorphous regions than in the crystalline regions due to the significantly higher chain mobility in the amorphous regions. The free radicals which exist in the amorphous regions disappear or "decay" by reacting rapidly with each other, often referred to as "recombining," to form neutral species having all electrons paired, which in other words is a covalent bond (cross-link). In contrast, free radicals (☆) in crystalline regions are

"trapped" by the immobility of crystals and thus often are prevented from reacting with other free radicals contained in the polymer chain. The space between chain segments within the crystal is greater than the length of a carbon-carbon bond. Accordingly, crystallites would need to "kink" in order for a bond to be formed between free radicals in crystallites. Such kinking is energetically disfavored, and therefore does not occur and results in "trapped" free radicals. A direct consequence of "trapped" free radicals in the crystalline region is their longer lifetime compared to free radicals in the amorphous region of the UHMWPE. Free radicals trapped in crystallites can persist for years, and the evidence to date indicates that such free radicals present oxidation targets as they abstract neighboring hydrogens and move along the polymer backbone.

12. If the irradiated UHMWPE is heated to melting, diminution to elimination of the crystalline state occurs (as schematically represented in slide 8 in the bottom middle of the slide), all of the polyethylene molecules will be mobile, thereby facilitating the recombination of free radicals and the creation of additional cross-links (●). By this approach, substantially all free radicals will recombine. Upon cooling, crystal regions will again form, although such crystals will be fewer in number, as schematically depicted in right bottom corner of slide 8.

13. Thus, when UHMWPE is heated to the melting point, all polymer chains will be in the mobile, amorphous form. Because the chains are mobile, there will be substantially no trapped free radicals. Upon cooling, new crystals will form, but the overall UHMWPE composition will have lower crystallinity. This was the first generation approach to solving the wear and oxidation problem by forming cross-linked UHMWPE, and then eliminating free radicals by melting, which results in a cross-linked UHMWPE that has a lower crystallinity than virgin UHMWPE. Products using this UHMWPE are Durasul® and Longevity®, which show decreased wear over time. See slide 9.

14. The first generation product is a stabilized product having lower crystallinity, but is more prone to fatigue crack propagation. Slide 10 shows that conventional UHMWPE (gamma sterilized at 25 kGy) is resistant to fatigue crack propagation, which markedly decreases upon aging. UHMWPE irradiated at a higher dose (100 kGy) initially shows decreased resistance to fatigue crack propagation, and that too markedly decreases upon aging. Irradiated (100 kGy) and melted UHMWPE has still lower initial resistance to fatigue crack propagation, but that resistance only slightly decreases upon aging, and hence the UHMWPE is stabilized against fatigue crack propagation.

15. Thus, the challenge has been to find a way to minimize the decrease in resistance of cross-linked UHMWPE to fatigue crack propagation that occurs during melting while stabilizing the UHMWPE against long-term oxidation.

16. Slide 11 concerns the use of vitamin E with UHMWPE. First, slide 11 shows the free radical cycle by depicting the reaction of a free radical with oxygen and hydrogen extraction, which is a continuing process that results in polymer scission. However, this cycle can be broken by using vitamin E (*i.e.*, α -tocopherol or T-OH). Vitamin E can donate a hydrogen to polymer free radicals and polymer peroxy free radicals to stop the scission cycle. After hydrogen donation, the vitamin E can react with itself to dimerize or can graft on to the polymer. What is important is that the polymer chain scission cycle is stopped by the protective effects of vitamin E.

17. However, the presence of vitamin E during irradiation can interfere with the formation of cross-links. See slide 12 (left side). This occurs when vitamin E reacts with a free radical prior to formation of a cross-link. The graph at the right side of slide 12 shows that samples treated with 0.3 wt% and 1.0 wt% of vitamin E will not achieve the optimum level of cross-link density, which is about 175 mol/m^3 . This level can be reached at the low level of 0.1 wt% of vitamin E with over 150 kGy radiation, but the combination of initial low vitamin E concentration and high radiation dose reduces the antioxidant efficiency of vitamin E and substantially compromises the long term protection of the polymer against

oxidation. For example, slide 13 shows that the effect of 100 kGy radiation on a 1.0 wt% level decreases vitamin E activity by about one third. Because free radicals can persist for years, any reduced antioxidant efficiency is problematic.

18. Slide 14 compares oxidation resistance of various samples initially and after 18 months of aging. The first group shows samples after 100 to 200 kGy irradiation for cross-linking. After 18 months aging, the surface oxidation, meaning the presence of free radicals, was very high (0.13 to 0.3 surface oxidation). The next group serves as a control, and was a blend of vitamin E and UHMWPE powder that was consolidated, but not irradiated and hence would not have appreciable free radicals. The final group was composed of blends of vitamin E and UHMWPE powder that were consolidated and irradiated at RT as in the prior art, and each showed an increase in surface oxidation after only 18 months. In this vein, it must be remembered that implants in the body are meant to last decades in order to avoid the need for revision surgery, and thus even greater oxidation can be expected over these significantly longer time periods.

19. According to our invention, the solution to the oxidation problem could be found by doping consolidated UHMWPE with vitamin E after irradiation-induced cross-linking. Vitamin E is an oily liquid substance that has a great affinity for UHMWPE, and allows a higher weight percentage of vitamin E to be soaked into the UHMWPE than achievable with other approaches. Slide 15 on the left shows a flask for doping. Upon doping at a given temperature, the Vitamin E will soak into the UHMWPE, with higher concentrations near the surfaces in the form of a gradient of lower concentration towards the interior bulk of a sample (5 mm depth of a 10 mm sample). Annealing of the sample will provide greater uniformity of the vitamin E throughout the sample. See slide 15 on the right. Adequate vitamin E levels will be present in the implant when the implant is in the body so that oxidation can be arrested over the long term, which deals with the problem of long-persisting "trapped" free radicals.

20. Slide 16 contains the data of slide 14, but also adds samples that were consolidated, irradiated and then doped with vitamin E (right side of graph). Both initially and after 18 months, these samples showed the lowest levels of surface oxidation for irradiated samples.

21. Slide 17 contains the data in slide 10, but also has a sample that was irradiated and then doped with Vitamin E (shaded). This sample shows greater fatigue resistance than the samples that were melted, but shows greater stability than the irradiated-only samples. Thus, the challenge discussed in paragraphs 14 and 15 above has been met. A stabilized UHMWPE that possesses (i) sufficient cross-linking for wear resistance, (ii) sufficient vitamin E activity for oxidation resistance, and (iii) greater fatigue crack resistance is provided for the first time by our invention, and cannot be achieved using the first generation product (see paragraphs 12-14 above) and the prior art vitamin E blends (see paragraphs 17-18 above).

22. Slide 18 provides the data. The first generation product (third row) has sufficient cross-linked density of 175 mol/m^3 , but has a low fatigue crack resistance of 0.51 to 0.54. The fifth row for blends shows a higher fatigue crack resistance (about 1.20), but a much lower cross link density of 73 mol/m^3 , and thus will be subject to wear and particle generation. See paragraph 17 and slide 12. The irradiated and vitamin E-doped sample (fourth row) has the ideal balance of properties in that it maintains a higher fatigue crack resistance while achieving a high enough cross-link density needed for wear resistance. Also enough vitamin E is within the doped sample so that it deals with the later effects of generated free radicals. See slide 19, which compares the wear resistance of an irradiated vitamin E blend (2 samples on the left) to irradiated and doped samples (2 samples on the right) that were subjected to terminal gamma sterilization. The latter two samples were able to maintain wear resistance.

23. Slide 20 shows the problems with vitamin E blends of the prior art. Blending UHMWPE with powder, consolidating and then irradiating will result in loss of Vitamin E potency to deal with free radicals during the aging process and lower levels of cross-linking that are needed to prevent the wear that forms the fine particles and causes osteolysis. If one were to work with powder but reverse the order of steps, a consolidated product could not be formed because cross-linking prevents consolidation.

24. Slides 21-23 discuss the advantages of annealing after doping with vitamin E by showing data from another experiment. First, slide 21 shows that after doping, vitamin E penetrates the surface and enters into the subsurface areas. The deepest regions, however, do not show sufficient levels of vitamin E, and thus are susceptible to oxidation in these regions. Slides 22 (vitamin E index vs. depth) and 23 (oxidation index vs. depth) shows that annealing the sample allows the vitamin E to more evenly distribute throughout the sample, and thereby provide oxidation resistance throughout the sample.

25. The vitamin E doping after irradiation approach is not found anywhere in the prior art. Rather, the prior art mixed polyethylene powder with vitamin E as a blend, and then subjected it to further treatments. Lidgren *et al*, U.S. Patent No. 6,448,315 discloses "antioxidant doping of UHMWPE particles" and that the "antioxidant ... is added to the UHMWPE powder." See column 4, lines 52-63. The doped powder of Lidgren is compression molded and irradiated. See column 7, lines 1-5. Parth *et al*, *J. Mat. Sci.* 13: 917-21 (2002) discloses the mixing of UHMWPE powder with α -tocopherol, followed by sintering for 7 hours at 220°C and 35 bar pressure to produce plates. Samples from the plates were then subjected to E-beam irradiation. See page 918, sections 2.1 and 2.2. Schaffner, U.S. Patent No. 6,277,390 discloses doping fine powder with low concentration of vitamin E followed by compression and then irradiation for sterilization. See column 2, line 59 to column 3, line 2. Each of these approaches will suffer from the problems noted in slide 20.

26. There are other approaches in the prior art, although quite distinct from our invention. Higgins, U. S Patent No. 5,753,182 discloses the use of pressurized hydrogen gas (H_2) to extinguish free radicals. Hydrogen (H_2) is the lightest known gas having a molecular weight of 2 g/mol, and is extremely flammable. The use of hydrogen is extremely dangerous and is not commercially practical, and therefore the Higgins approach, to my knowledge, has not found its way into commercial practice. Moreover, due to its extremely low molecular weight and gaseous nature, hydrogen gas will not persist in the UHMWPE and thus cannot be distributed throughout the UHMWPE implant prior to and after implantation. Rather, the hydrogen gas will evolve out of the Higgins polyethylene. Accordingly, hydrogen will not maintain a distribution and presence in a UHMWPE implant to address the long-term oxidation threat posed by trapped free radicals. Thus, Higgins' use of hydrogen gas does not teach or suggest our invention that utilizes vitamin E.

27. Hahn, U.S. Patent No. 5,827,904, discloses "beta carotene doped UHMWPE powder." See column 3, lines 38-40. This doped powder was melted and compressed using a piston. See column 5, lines 7-17. Doping of stock UHMWPE with beta carotene also is mentioned. See column 3, line 15. However, Hahn does not disclose annealing. Moreover, beta carotene is a solid and must be dissolved in an organic solvent, like cyclohexane or isopropyl alcohol, prior to doping. See Column 2 and Example 2 of Hahn. Hahn does not discuss what happens to the solvent and polymer after doping. If the solvent remains in the polyethylene to keep the beta carotene in solution, the presence of the solvent could have an adverse effect on the polymer. If the solvent elutes or evaporates out of the polyethylene, the beta carotene could revert to a crystalline structure and not be available to react with trapped free radicals. Finally, residual solvent (*i.e.*, cyclohexane or isopropyl alcohol) could elute out during or after implantation and result in an adverse tissue response to the solvent. Hahn provides no answers to these scenarios.

28. Significantly, Hahn states that beta carotene “can participate in both anti-oxidant as well as pro-oxidative processes”. See column 45-46. Irradiation and cross-linking caused by irradiation also are not discussed by Hahn, and thus Hahn does not deal with the challenges posed by the high irradiation needed for cross-linking to prevent wear. Accordingly, the skilled person reviewing Hahn would not look to beta carotene to meet the free radical problem posed by higher levels of irradiation.

29. Additionally, Hahn’s approach must be considered in view of a later article by Hahn *et al.*, published in *J. Biomed. Mat. Res.* 35: 31-37 (1997). Hahn tested UHMWPE knee replacements retrieved from revision surgeries. See article at page 32, left column, table 1 and associated text. Conventional UHMWPE implants at that time (initially implanted in the late 1980’s to the early 1990’s) would have been terminally gamma sterilized and thus cross-linked to a degree and contain free radicals. Hahn observed beta carotene on UHMWPE debris in the retrieved implants, and mentioned that beta carotene is found in the bone. See page 32, right column, 4th full paragraph; page 33, right column, 1st full paragraph; page 34, right column 3rd full paragraph. Hahn questions whether there might be a role for beta carotene from the body in mitigating degradation, but provides no approach how to utilize this possibility to avoid degradation. See paragraph bridging pages 35-36. Accordingly, Hahn’s association of body-generated beta carotene with debris and wear from implants, combined with various uncertainties attendant with Hahn’s approach, means that the Hahn patent does not suggest that doping UHMWPE with an antioxidant like vitamin E would be useful. Because beta carotene was not sufficient to stop debris as found by Hahn *et al.*, the totality of Hahn’s work provides no reason to try other compounds.

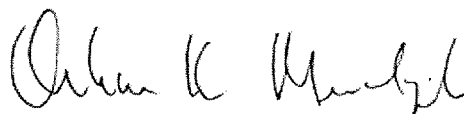
30. Hahn’s reliance on beta carotene, which requires an organic solvent and has both anti-oxidant and pro-oxidant properties, would not direct the skilled person towards vitamin E. Hahn’s findings that beta carotene is present in debris would discourage the skilled person from doping implants with antioxidants generally, and thus direct the skilled person away from vitamin E. Finally, Hahn does not disclose nor suggest any type of annealing step to prevent oxidation throughout the bulk of UHMWPE.

31. In sum, Lidgren, Parth, Schaffner, Higgins and Hahn, alone or in combination, neither teach nor suggest the invention as claimed. Only the present invention can achieve the balance of wear resistance, oxidation resistance and fatigue crack resistance discussed above and shown in slides 15-19.

I declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements and the like are made with knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of this application or any patent issuing thereon.

Tuesday, August 05, 2008

Date



Orhun K. Muratoglu, Ph. D.

CURRICULUM VITAE

DATE PREPARED: July 16, 2008

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Education:

- 1991 B.S. (Materials Science and Engineering), Rensselaer Polytechnic Institute of Technology
1995 Ph.D. (Materials Science and Engineering, Program in Polymer Science and Technology), Massachusetts Institute of Technology

Academic Appointments:

- 1995- Research Affiliate, Massachusetts Institute of Technology, Cambridge, MA
1995-2002 Instructor in Orthopedic Surgery, Harvard Medical – Orthopedic Surgery, Boston, MA
2002-2005 Assistant Professor of Orthopedic Surgery, Harvard Medical School – Orthopedic Surgery, Boston, MA
2005- Associate Professor of Orthopedic Surgery, Harvard Medical School – Orthopaedic Surgery, Boston, MA

Hospital or Affiliated Institution Appointments:

- 1995-2002 Assistant Bioengineer, Orthopaedic Surgery, Massachusetts General Hospital, Boston, MA
1995-2002 Research Affiliate, Department of Chemical Engineering, Massachusetts Institute of Technology, Cambridge, MA
2001-2004 Deputy Director, Orthopedic Biomechanics and Biomaterials Laboratory, Massachusetts General Hospital, Boston, MA
2001- Alan Gerry Scholar, Massachusetts General Hospital, Boston, MA
2004- Co-Director, Orthopedic Biomechanics and Biomaterials Laboratory, Massachusetts General Hospital, Boston, MA

Professional Societies:

- 1990- Materials Research Society, Member
- 1990- American Chemical Society, Member
- 1995- American Institute of Chemical Engineers, Member
- 1995- Society for Biomaterials, Member
- 1996- American Society for Testing and Materials, Member
- 1997- Orthopaedic Research Society, Member
- 2000- American Academy of Orthopaedic Surgeons, Member
- 2003- American Academy of Hip and Knee Surgeons, Member

Editorial Boards:

- 1997- Ad-Hoc Reviewer, Clinical Orthopaedic and Related Research
- 1997- Ad-Hoc Reviewer, Journal of Biomedical Materials Research
- 1997- Ad-Hoc Reviewer, Biomaterials
- 2001 Ad-Hoc Reviewer, Austrian Science Fund
- 2003- Ad-Hoc Reviewer, Journal of Orthopaedic Research
- 2005- Ad-Hoc Reviewer, Polymer
- 2006- Ad-Hoc Reviewer, US-Israel Bi-national Science Foundation (BSF)

Awards and Honors:

- 1989-1990 Dean's List, Rensselaer Polytechnic Institute
- 1991 Summa cum Laude, Rensselaer Polytechnic Institute
- 1991 PPST Fellowship, Massachusetts Institute of Technology
- 1991 Matthew Albert Hunter Prize for Outstanding Academic Achievement, Rensselaer Polytechnic Institute
- 1992 Dupont Fellowship, Massachusetts Institute of Technology
- 1995 First Prize, Hoechst Celanese Polymer Poster Competition, Massachusetts Institute of Technology
- 1995 Summa cum Laude, Massachusetts Institute of Technology
- 1998 Best Paper Award, Montreal RETEC '97 Society of Plastics Engineers
- 1999 HAP Paul Award, International Society for Technology in Arthroplasty
- 2000 Partners in Excellence Award, Massachusetts General Hospital
- 2001 Marshall R. Urist Young Investigator Award, American Academy of Orthopaedic Surgeons
- 2006 HAP Paul Award, International Society for Technology in Arthroplasty

a. Invited Presentations

Invited Lectures

International Invited Lectures

- 2000 Invited Lecture: Highly crosslinked polyethylene in total joints at the 27th Annual Meeting, Japanese Hip Society, Nagoya, Japan
- 2000 Invited Lecture: European Knee Osteoarthritis Week, Arthroplasty Symposium, University of Ulm, Germany
- 2000 Invited Lecture: Irradiated and melted UHMWPE tibial knee inserts at the 85th National Congress, Torino, Italy, Italian Society of Orthopaedics and Traumatology

- 2000 Invited Lecture: Radiation crosslinked UHMWPE for total knees at the 2nd Harlaching Spring Symposium, Academic Hosp Munchen-Harlaching, Munich, Germany
- 2000 Invited Lecture: Residual free radicals in UHMWPE. Whistler 2000 Orthopaedic Symposium, Whistler, British Columbia, Zimmer
- 2001 Invited Lecture: Highly crosslinked polyethylenes in total joints at the Osteologie in Forschung und Praxis -Der Osteoblast, University of Wurzburg, Wurzburg, Germany
- 2001 Invited Lecture: In vitro testing of highly crosslinked total knees at the Triennial Congress, Asian Pacific Orthopaedic Association, Adelaide, South Australia
- 2002 Invited Lecture: Radiation chemistry in improving wear and oxidation resistance of UHMWPE - 3rd Annual Turkish Arthroplasty Meeting, The Association of Turkish Arthroplasty Surgeons, Antalya, Turkey
- 2003 Invited Lecture: The effect of third body particles on in vivo wear of crosslinked acetabular liners at the Satellite Symposium, European Orthopaedic Research Society, Helsinki, Finland
- 2003 Invited Lecture: The state-of-the-art of crosslinked UHMWPEs in orthopedics at the Annual Meeting, European Federation of National Associations of Orthopaedic and Traumatology, Helsinki, Finland
- 2004 Invited Lecture: Limitations of contemporary crosslinked polyethylenes and potential 2nd generation solutions, Peter Herberts Festchrift, Sahlgrenska University Hospital, Goteborg, Sweden
- 2004 Invited Lecture: Materials Science in Orthopaedics: Low-Wear, High Fatigue Polyethylenes for Total Joints, Biomed Meeting, Ankara, Turkey
- 2005 Invited Lecture: The effect of alpha-tocopherol on the wear of radiation crosslinked UHMWPE, Oxidative Stabilization of UHMWPE, Turin, Italy
- 2005 Invited Lecture: Alpha-tocopherol stabilized irradiated acetabular liners, UHMWPE for arthroplasty: degradation, stabilization and crosslinking, Turin, Italy
- 2005 Invited Lecture: Second Generation Highly Crosslinked UHMWPE for Total Joint Arthroplasty, SICOT, Istanbul, Turkey
- 2006 Invited Lecture: Radiation Chemistry of Polyethylenes for Total Joint Application, IRaP, Antalya, Turkey
- 2006 Invited Lecture: Presidential Guest Lecturer: New Horizons in Polyethylene Technology, European Hip Society, Antalya, Turkey

National Invited Lectures

- 1995 Invited Lecture: The effects of gamma sterilization on UHMWPE. Workshop on Polyethylene, Combined Orthopaedic Research Society
- 1998 Invited Lecture: The effect of crosslinking on wear at the Material Science and Engineering Colloquium Series, Ohio State University
- 1999 Invited Lecture: Seminar Series at the Mechanical Engineering, Aeronautical Engineering and Mechanics, Rensselaer Polytechnic Institute
- 1999 Invited Lecture: Hip simulator wear studies at the Hip, Knee, and Shoulder Symposium, University of Florida

- 2000 Invited Lecture: High cycle wear testing of highly crosslinked UHMWPE acetabular liners at the Hip, Knee, and Shoulder Symposium, University of Florida
- 2000 Invited Lecture: Wear 2000 Workshop, Orthopaedic Research Society
- 2000 Invited Lecture: Low wear and low oxidation with irradiated and melted UHMWPE at the Wear 2000 Workshop, American Academy of Orthopaedic Surgeons and National Institute of Health
- 2001 Invited Lecture: Workshop on Ultra-high molecular weight polyethylene , Society for Biomaterials
- 2001 Invited Lecture: New Test Methods for Evaluating the Performance of Conventional and Crosslinked UHMWPE , American Society for Testing and Materials
- 2001 Invited Lecture: Analysis of explanted highly crosslinked UHMWPE at the Tribology Issues in Biology and Medicine, Argonne National Laboratory
- 2002 Invited Lecture: Overview of radiation chemistry of UHMWPE for orthopedics at the Grand Rounds, University of Oklahoma College of Medicine
- 2002 Invited Lecture: Surface Analysis of Early Retrieved Acetabular Polyethylene Liners, American Society for Testing and Materials
- 2002 Invited Lecture: Overview of radiation chemistry of UHMWPE for orthopedics at the Grand Rounds, University of Utah
- 2002 Invited Lecture: Highly crosslinked polyethylenes in total hip and total knee at the Hip, Knee, and Shoulder Symposium, University of Florida
- 2002 Invited Lecture: Effect of Crosslinking on the Delamination and Adhesive Wear Behavior of Tibial Knee Inserts, The Knee Society Meeting, American Academy of Hip and Knee Surgeons
- 2003 Invited Lecture: Update on highly crosslinked polyethylenes in total hip and total knee at the Hip, Knee, and Shoulder Symposium, University of Florida
- 2003 Invited Lecture: E-beam crosslinked and melted polyethylene, Alternate bearing surfaces in total joint replacement, University of Pennsylvania Medical Center
- 2003 Invited Lecture: Highly crosslinked polyethylene in total knees: Another view, Alternate Bearing Surfaces in Total Joint Replacement, University of Pennsylvania Medical Center
- 2003 Invited Lecture: Highly crosslinked polyethylene in total knees: Another view, Alternate bearing surfaces in total joint replacement , University of Pennsylvania Medical Center
- 2003 Invited Lecture: E-beam crosslinked and melted polyethylene, Alternate bearing surfaces in total joint replacement, University of Pennsylvania Medical Center
- 2004 Invited Lecture: Update on highly crosslinked polyethylenes in total hip and total knee at the Hip, Knee, and Shoulder Symposium, University of Florida
- 2004 Invited Lecture: Radiation crosslinked and melting of polyethylene, Hip, Knee and Shoulder Symposium, University of Pennsylvania Medical Center
- 2004 Invited Lecture: Diminished Polyethylene wear using a highly crosslinked polyethylene, The Knee Society Meeting, American Academy of Hip and Knee Surgeons
- 2005 Invited Lecture: Vitamin E Stabilized, Irradiated UHMWPE for TKR, Advances in Hip and Knee Arthroplasty Meeting, Washington DC

- 2005 Keynote Presentation: Improving the Wear Resistance of Ultra-high Molecular Weight Polyethylene (UHMWPE), World Tribology Congress, Washington DC
- 2005 Invited Panel Discussion: Alternate Bearing Surfaces, 20th Annual Vail Orthopaedic Symposium, Vail, Colorado
- 2006 Invited Lecture: Crosslinked UHMWPE in Total Knees, ISTA Meeting, New York, NY
- 2007 Grand Rounds at Dartmouth: Second Generation Highly Crosslinked UHMWPEs, Hanover NH

Regional Invited Lectures

- 2002 Invited Lecture: Crosslinked polyethylenes at the Fall Meeting, New England Orthopaedic Society
- 2004 Invited Lecture: Second Generation Crosslinked Polyethylenes for Total Joints at the Traveling Fellow Program AOA Presentation, Massachusetts General Hospital
- 2004 Invited Lecture: Current and Future Crosslinked Polyethylenes, How Good are They?, American Orthopaedic Association
- 2005 Keynote Speaker: Crosslinked polyethylenes, Harvard Hip Course, Harvard Medical School
- 2006 Invited Lecture: Polyethylene: New Perspectives at the Traveling Fellow Program AOA Presentation, Massachusetts General Hospital
- 2006 Invited Lecture: Second Generation Polyethylene, Harvard Hip Course, Harvard Medical School.
- 2006 Invited Presentation: Cross-Linked Polyethylene for the Knee, Harvard Hip Course, Harvard Medical School.

Plenary Presentation

- 1998 Plenary Presentation: Effect of Crosslinking on Wear of Polyethylene, Gordon Conference on Tribology

Bibliography

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